REMARKS/ARGUMENTS

Claims 62, 64-65, and 67-70 are pending in the present case.

Claim Rejection under 35 U.S.C. § 112:

Claims 62, 64-65, and 67-68 are rejected under 35 U.S.C. § 112, first paragraph, on the ground that the Specification does not reasonably provide enablement for using any or all inactivated or attenuated virus to induce a serum immune response in a CD4+ T cell deficient animal and human. The Examiner asserts that the Specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicants respectfully traverse these rejections.

The claimed invention is based on the inventors' actual data that formalin-inactivated intact influenza virus induced antibody production in mice lacking functional CD4+ T cells. Furthermore, these antibodies showed neutralizing activity against live influenza virus *in vivo* and *in vitro*, and the CD4+ deficient mice, upon immunization with inactivated influenza virus, were protected from intranasal challenges with lethal doses of live influenza virus.

Applicants emphasize that these studies were the first demonstration that it is possible to immunize a subject deficient in CD4+ T cells (i.e., immunocompromised) to provide protection against various viral pathogens. These findings were unexpected because the state of the art at the time was such that it was believed that vaccinating these immunocompromised subjects would not be effective. The prevailing theory in the art was that the CD4+ T helper cells are essential for inducing an antibody response as discussed in Oxenius *et al.* (*Adv. Immunol.* 1998 70:313) and Parker, D.C. (*Annu. Rev. Immunol.* 1993 11:331 [of record herein]).

The Examiner merely states that the Specification is enabling for using a formalin inactivated influenza virus P8/5 to induce an immune response in a mouse model but does not provide enablement for using any and all inactivated or attenuated virus to induce a serum immune response in a CD4+ deficient animal or human.

Applicants do not agree. There is no objective scientific reason why a skilled artisan would not expect that any attenuated or inactivated virus can induce an immune response in a CD4+ T cell deficient subject as was demonstrated in the Specification using influenza virus as an example. Applicants request that the Examiner provide such evidence.

Based on the foregoing, withdrawal of the rejection under 35 U.S.C. § 112 is respectfully requested.

Claim Rejection under 35 U.S.C. § 102:

Claims 62, 64-65, 67-68 and 70 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by either Compans *et al.* (United States Patent No. 4,790,987), Murphy *et al.* (*Vaccine* 1990 8:497), Muster *et al.* (*J. Virol.* 1994 68:4031), Li *et al.* (*J. Virol.* 1993 67:6659), Pales *et al.* (*J. Inf. Dis.* 1997 176:S45) or Budowsky *et al.* (*Vaccine* 1993 11:343). Applicants respectfully traverse these rejections for the following reasons.

The claimed invention is a method for inducing a humoral immune response in a CD4+ T cell deficient subject by administering an immunogenic composition comprising an inactivated intact virus such that the subject is protected from such viral pathogens.

None of the cited references teaches the invention. Compans *et al.* teaches a vaccine composition containing virus subunits derived from an intact virus. The vaccination studies described therein used the formalin-inactivated influenza virus. However, the animals vaccinated were female hamsters which are immunologically intact, i.e., not deficient in CD4+ T cells. This is consistent with the prevailing belief in the art at the time that an effective vaccination requires the presence of CD4+ T cells as discussed above. There is no teaching or suggestion that an immunization of a CD4+ T cell deficient animal with an intact inactivated virus will provide protective immunity as taught in the present application.

The shortcomings of the remainder of the cited art have been discussed in the previous Response filed on July 3, 2003. For example, Murphy *et al.* describes a method for immunization with an inactivated RSV or purified F glycoprotein in cotton rats. Muster *et al.* describes an immunization study using a chimeric influenza virus containing a HIV peptide epitope in mice. Li *et al.* describes the use of chimeric influenza virus expressing an epitope of HIV to induce antibodies in mice. Pales *et al.* describes several approaches to induce a more effective immune response against an HIV epitope using various recombinant influenza virus vaccines in mice. Budowsky *et al.* describes effects of inactivation of viral components by beta-propriolactone on inducing an immune response in mice.

Applicants point out that the animals, either rats or mice, employed in the studies of the cited references were not deficient in CD4+ T cells. Accordingly, none of the cited art teaches the invention as claimed herein. There is no teaching that the CD4+ T cell deficient animals can be effectively immunized using an intact inactivated or attenuated virus.

In summary, none of the cited art teaches each and every limitation of the claimed invention. Therefore, the invention is not anticipated by any of the cited art. Contrary to the Examiner's allegation, applicants maintain that the invention is a new use of a known composition. The new use was discovered only after the inventor's studies in the CD4+ T cell deficient mice. Without this information, the concept of providing protective immunity in a subject deficient in CD4+ T cells would not have become a reality. The invention was made only after the actual demonstration by the inventors. Accordingly, withdrawal of the rejection under 35 U.S.C. § 102 is respectfully requested.

Conclusion:

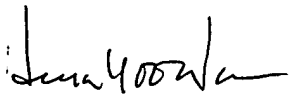
It appears that claim 69 is allowable. Based on the foregoing remarks and arguments, all the claims in the present application are considered to be in condition for allowance. Passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone call is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This Amendment is accompanied by a Petition for Extension of Time (one month) and a check in the amount of $ 55.00 as required under 37 C.F.R. 1.17(a)(1) for a small entity.

However, if the amount submitted is incorrect, please charge any deficiency or credit any overpayment to Deposit Account No. 07-1969.

Respectfully submitted,



Heeja Yoo-Warren
Reg. No. 45,495

GREENLEE, WINNER AND SULLIVAN, P.C.
5370 Manhattan Circle, Suite 201
Boulder, CO 80303
Telephone: (303) 499-8080
Facsimile: (303) 499-8089
E-mail: winner@greenwin.com
Attorney Docket No. 96-99
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